REMARKS

Careful consideration has been given to the Official Action of July 11, 2006 and reconsideration of the application as amended is respectfully requested.

CLAIM REJECTIONS

Claims 3-9 and 11 are rejected under 35 U.S.C. 112, second paragraph.

Claims 1-14, 16-68, 103-114, 116-137, 176, 178, 209-210 and 212 are rejected under 35 U.S.C. 102(b) as being anticipated by Schalkhammer et al (U.S. 5,866,433).

Claim 211 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schalkhammer et al.

CLAIMS AMENDMENTS AND ARGUMENT

Amendatory action has been taken in the claims to relieve them from the rejection under 35 U.S.C. 112 and to emphasize features and characteristics by which the claims distinguish over the cited art. The Amendatory Action taken in the claims only clarifies existing limitations and does not raise new issues requiring further consideration and/or search by the Examiner. It is especially emphasized that this is the case for the distinctive features (a) – (e) recited hereafter in paragraph 2.2, except for feature (c) reciting *applying said electromagnetic radiation from said external source to a second structure* **with a sample**. However, this feature is introduced solely to clearly clarify the difference between the invention and the cited patent even though without this recitation the differences between the invention and the cited patent are sufficient to consider Claim 1 as patentable over this reference.

With respect to the rejection under 35 U.S.C. 112 it appears that in the first step the word "transmitting" was inadvertently cancelled thereby creating the 112 problem in the rejected claims. By reinserting the word "transmitting" not only is Claim 1 corrected but additionally the dependent claims now find antecedent support for the language therein. The amendment of Claim 1 now makes it consistent with the other independent claims and with the prior versions thereof.

In connection with the Examiner's rejection of Claims 1-14, 16-68, 103-114, 116-137, 176, 178, 209-210 under 35 U.S.C. 102(b) as being anticipated by Schalkhammer et al. (US 5,866,433) the following should be noted:

2.1 US' 433 discloses a sensor for measuring an analyte concentration based on the use of a transparent substrate carrying an array of metallic islands and a biorecognitive layer selected to adsorb the dissolved analyte. According to this technique, **a certain analyte-specific fluorescent compound must be provided** to bind the analyte that is to be adsorbed. This fluorescent compound is provided in the solution during the measurement. The technique is based on such a property of the selected fluorophor that its quantum yield or **its fluorescence spectrum is significant only in the vicinity of the island layer**.

2.2 According to the Examiner's interpretation (see page 7 paragraph last but one of the Detailed Action where the Examiner comments to the Applicant's arguments in par. 1.2 submitted in reply to the previous Office Action), *"The Office maintains '422 teaches fluorophors are excited and emit radiation which has been properly read on the instant claims"*.

However, US ' 433 does not disclose a combination of features of Claim 1 of the present application, at least because it does not disclose such features of the invention as:

(a) applying electromagnetic radiation of a predetermined wavelength range from an external source to a first structure for transmitting said electromagnetic radiation of said predetermined wavelength range through the first structure,

(b) detecting a transmission of said electromagnetic radiation of said predetermined wavelength range through said first structure,

(c) applying said electromagnetic radiation form said external source to a second structure with a sample for transmitting said electromagnetic radiation of said predetermined wavelength range through said second structure and through the sample applied thereto;

(d) detecting said electromagnetic radiation of said predetermined wavelength range passed through said second structure and through said sample, and

(e) comparing measurements of the surface plasmon absorption of the first and second structures.

2.3 The technique of US ' 433 relies on the following method (col. 2, lines 12-37):

"A method of the invention for measuring the concentration of at least one analyte in a sample thus comprises the steps of;

(a) contacting the sample with a biorecognitive sensor layer which is applied on or in close vicinity of at least one island layer consisting of islands of electrically conductive material,

(b) contacting the sample with an analyte-specific fluorescent compound of low quantum yield,

(c) binding the analyte-specific fluorescent compound to the analyte, which in turn is bound by the biorecognitive layer, the quantum yield of the analyte-specific fluorescent compound increasing strongly in the vicinity of the island layer,

(d) radiating excitation radiation which is suitable for excitation of the analyte-specific fluorescent compound into the at least one island layer,

(e) determining the fluorescence radiation emitted by the bound analyte-specific fluorescent compound as a measure for the analyte concentration.

As an alternative to item (c), both the analyte-specific fluorescent compound and the analyte to be measured are bound by the biorecognitive layer, the quantum yield of the analyte-specific fluorescent compound again increasing strongly in the vicinity of the island layer".

It is thus clear that the method disclosed in US '433 does not teach transmission of externally to structures generated electromagnetic radiation of a predetermined wavelength range, transmitting said radiation through the structures, and detection of said predetermined wavelength range transmitted through the structure, and does not teach performance of two measurements on two different structures, respectively. US '433 teaches performing only one measurement for determination of the analyte concentration. This single measurement is disclosed in step (e) and is performed when the analyte-specific fluorescent compound is bound by the biorecognitive layer, indirectly, as in step (c), or directly, as in the step's (c) alternative. Thus, US ' 433 does not disclose features (a), (b) and (e) (reciting "comparing") of the list of features of Claim 1 in section **2.2** above.

2.4 Additionally, it should be noted that US '433 teaches away from utilizing more than one measurement for the determination of the analyte concentration because the inventors of US ' 433 consider the possibility of using only one single measurement of the fluorescence as the advantage of this technique. In fact, the technique of US ' 433 utilizes an effect of the change of fluorescence in which the starting fluorescence is essentially zero. This is clear from col. 2 line 55 to col. 3 line 3 reciting:

"In conventional fluorescence sensors fluorophors with a high quantum yield must be employed to guarantee the necessary sensitivity of the sensor. On the other hand dissolved fluorescent molecules in the sensor environment will produce a strong background signal limiting the sensitivity of the measuring system. To obtain a satisfactory signal-to-noise ratio, excess fluorophor solutes must be removed from the sensor prior to measurement. The new type of optochemical fluorescence sensor described by the invention does not have this disadvantage since the dissolved molecules exhibit a very low intrinsic fluorescence which will strongly increase only after bonding to the biorecognitive layer. As a consequence, the biorecognitive bond can be measured immediately and selectively at the surface of the sensor without separation of the analyte solution, which is not possible in conventional sensors".

2.5 The feature (e) of the list of features of Claim 1 in section **2.2** above is not disclosed in US '433 because the technique of US ' 433 does not include measuring the surface plasmon absorption.

It should be noted that the effects of a change of absorption and of a change of fluorescence are distinguished in US '433. For example, US '433 recites (col. 1 lines 11-17): *"Optochemical sensors are based on the fact that a chemical reaction between the sensor material and the analyte leads to a change in the optical properties of the sensor. Such a change may concern optical properties such as absorption or fluorescence intensity; as a consequence, the reaction may be detected by means of spectroscopic methods".*

Further, US '433 explains that its technique is based on the measurement of the fluorescence. See for example col. 3 lines 4-6 reciting: *"It will thus be possible to observe a change in optical properties, such as fluorescence intensity or the fluorescence spectrum, after a comparatively short response time"*, and also col. 4 lines 12-14 reciting *"Due to the thinness of the layer and the short response time resulting therefrom, the increase in fluorescence intensity can be detected quickly and reliably"*.

In col. 3 lines 55-59, US '433 teaches away from using any absorption of the fluorescent light: *"A particularly strong increase in fluorescence intensity is observed if the diameter of the islands is appreciably smaller than the wavelength of the light used for monitoring and evaluation, and if the absorption minimum overlaps with the emission maximum of the fluorophor"*. In particular it is clear that US '433 teaches away from using plasmon resonance.

In col. 3 lines 15-23, US '433 teaches away from using conventional method of interferometry or surface plasmon resonance in thin layers:

"By means of conventional methods of interferometry or surface plasmon resonance, slight chemical changes in thin layers may be detected only with the use of complex measuring equipment. It has been found quite unexpectedly that a much simpler measuring configuration is obtained, in addition to greater sensor sensitivity, if the island layer is applied on a transparent surface and is used for coupling in the measuring beam (e.g., laser or LED)".

The above quote in no way implies that the technique of US '433 utilizes interferometry, plasmon resonance, or plasmon absorption of the fluorescent light. It is clear that the technique of US '433 is incapable of using for example such method as interferometry: the fluorescent light is not coherent. It should be understood that the method of the present invention is also different from conventional interferometry or plasmon resonance. In particular, the present application recites *"Compared with related techniques, the present method does not require complicated and expensive instrumentation (as in surface plasmon resonance spectroscopy, SPR)"*.

As well, US' 433 does not disclose features (c) and (d) of the list of features of Claim 1 (see section **2.2** above). This is because the techniques of US' 433 and of the present invention utilize different light propagation schemes: while the invention can utilize the transmission of light through the structure and the sample and the detection of thusly passed light, the technique of US '433 cannot utilize the transmission of light through structure and the sample and the detection of thusly passed light.

In fact, according to the technique of US' 433, the detected light essentially does not include light passed through the sample. Rather, the detected light is the fluorescent light excited by the fluorescent material bound directly or indirectly to the biorecognitive layer and passed only through the part of the structure that does not include a sample to be inspected. Indeed, see col. 3 lines 46-50: *"Due to the measuring geometry of the optical biosensor, the excitation light can be radiated into the transparent side of the sensor which is not in contact with the sample and the emitted fluorescent photons may be measured at the maximum solid angle on the same side"*. The transmission of fluorescent light through the structure and through the sample is excluded, because the fluorescent light is generated in between the structure and the sample, and it can pass only through one of these.

As for the technique of the present application, see for example the following paragraph (page 45, lines 5-15): *"System 10 comprises a source of electromagnetic radiation 12. Source 12 is more typically a light or laser source. If the electromagnetic radiation is in the visible light range, then a filter monochromator 14 is normally essential in system 10. In contrast, if the radiation is laser radiation, then no filter monochromator is required. Radiation is typically passed from source 12 via filter monochromator 14 to a sample holder 16 into/onto which a sample 19 is placed. The incident radiation is transmitted through sample 19 to a detector 18"*. Also, please see the following paragraph (page 45 lines 16-20) *"Additionally, the radiation may be reflected from sample 19 to detector 18. Radiation may be passed through sample 19 prior to adsorption of a chemical thereto and following adsorption thereto (as is described hereinabove in FIGS. 1A and 1B)"*.

2.6 In view of the above arguments, it should be clear that the other independent claims 103, 209-211 are also patentable over US' 433. In particular US' 433 does not disclose detection of "transmission profile". Also, with regards to the apparatus and kit claims, US '433 does not disclose the combination of features recited in these claims. Configuration of measurement apparatuses is different in US '433 and in the present invention. US '433 does not disclose at least the following features of the apparatus claim:

(i) an external transmitter configured and operative to transmit the electromagnetic radiation of the predetermined wavelength range through the structure

(ii) a processor operative to receive the measurement of the structure transmission profiles of the electromagnetic radiation to be transmitted by said transmitter for the first structure and for the second structure with the sample, analyze the transmission profiles of the structures under measurements.

In connection with the feature (i), we refer to Figs. 1A-1C of the present application, clearly showing the use of external light source. Moreover, as seen in the figures, the invention can use a spectral filter (monochromator) in between the light source (transmitter) and the sample, which cannot be used in US '433. In US '433 the transmitter is a fluorescent material on the structure.

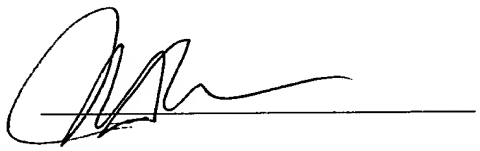
2.7 It is clear that the techniques of US' 433 and of the present invention utilize different sources of radiation to be detected and analyzed: according to US' 433, this is a fluorescent material on the structure, and according to the invention this is an external light source illuminating the structure. In this connection, the Examiner's attention should be drawn to the fact that the claims clearly recite that the detected light is said light of said predetermined wavelength which illuminates the structure. It can be understood that the use of an external light source provides for externally controlling the process under inspection, while according to US' 433 the internal source of the detected light is used.

2.8 Moreover, it is clear from the present application that the invention does not rely on the use of fluorescent material – see for example page 76 lines 19-26 stating that: *"Examples of chemical substance-metallic islands moiety 65 include self assembled monolayer (SAMs) of 1. The use of the surface plasmon intensity change (or PIC) for studying self-assembly of* ***molecules that do not absorb light in the UV/visible/IR range*** *is exemplified by monitoring the adsorption kinetics of a monolayer of 1 (which is transparent in the visible region), as shown in FIG. 11A hereinabove."* This is also repeated on page 65 lines 10-15 of the application as filed.

It is therefore respectfully submitted that Schalkhammer et al., is not applicable to the claims under 35 U.S.C. 102. As the claims express limitations not found nor remotely suggested in Schalkhammer and, which produce entirely distinctive results. This also applies to Claim 211 and therefore, the rejection under 35 U.S.C. 103 is not believed tenable.

Favorable reconsideration of the application and allowance of the claims is therefore earnestly solicited. If the Examiner intends to reject the claims again, it is requested that the Examiner telephone the undersigned attorney to resolve any outstanding issues.

Respectfully submitted,



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